SUMMARY OF PRODUCT CHARACTERISTICS

LOSARGOOD AM H (Losartan Potassium 50 mg, Amlodipine 5 mg and Hydrochlorothiazide 12.5 mg Tablets)

1. NAME OF THE MEDICINAL PRODUCT

LOSARGOOD AM H (Losartan Potassium 50 mg, Amlodipine 5 mg and Hydrochlorothiazide 12.5 mg Tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 50 mg losartan potassium USP, 5 mg amlodipine besylate USP equivalent to amlodipine, and 12.5 mg hydrochlorothiazide USP.

Excipients with known effect:

Each tablet contains 30.00 mg of lactose monohydrate. For warnings, see section 4.4.

Each tablet contains sunset yellow (E110) as a colouring agent. For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Orange-coloured, round, biconcave-shaped, film-coated tablet, plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LOSARGOOD AM H is indicated for the treatment of hypertension, as substitution therapy in adult patients whose blood pressure is already controlled with the combination of losartan, amlodipine and hydrochlorothiazide taken as individual components or as dual combinations.

4.2 Posology and method of administration

Adults

The usual recommended dose is one tablet once daily. The dose may be increased to 2 tablets once daily if blood pressure control is inadequate after 1–2 weeks.

Special populations

Hepatic impairment:

Losartan should not be administered in patients with severe hepatic impairment (see section 4.4). Amlodipine should be titrated slowly in patients with severe hepatic impairment. This fixed-dose combination is not recommended in patients with hepatic impairment.

Renal impairment:

Caution is required in patients with renal impairment. Hydrochlorothiazide may be ineffective at low creatinine clearance. Losartan should be used with caution in patients with bilateral renal artery stenosis. This fixed-dose combination is not recommended in patients with severe renal impairment (creatinine clearance <30 ml/min).

Elderly:

Blood pressure reduction may be more marked in the elderly. Particular care is needed. No specific dose adjustment is required, but amlodipine clearance may be reduced in the elderly.

Paediatric population:

The safety and efficacy of this fixed-dose combination in children has not been established.

Method of administration

Oral. Tablets may be taken with or without food, at approximately the same time each day.

4.3 Contraindications

- Hypersensitivity to any component of this product (including other sulfonamide-derived drugs — hydrochlorothiazide is a sulfonamide).
- Anuria.

- Concomitant use with aliskiren in patients with diabetes mellitus.
- Second and third trimester of pregnancy (losartan and hydrochlorothiazide components).
- Severe hepatic impairment.

4.4 Special warnings and precautions for use

Losartan — Hypersensitivity and angioedema

Patients with a history of angioedema (swelling of the face, lips, throat and/or tongue) should be closely monitored.

Losartan — Hypotension and electrolyte/fluid imbalance

Symptomatic hypotension, especially after the first dose and after increasing the dose, may occur in patients who are volume- and/or sodium-depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. These conditions should be corrected prior to administration or a lower starting dose should be used.

Losartan — Electrolyte imbalances

Electrolyte imbalances are common in patients with renal impairment, with or without diabetes. In diabetic nephropathy patients, the incidence of hyperkalaemia was higher with losartan than with placebo. Plasma potassium concentrations and creatinine clearance values should be closely monitored. Concomitant use of potassium-sparing diuretics, potassium supplements or potassium-containing salt substitutes with losartan is not recommended.

Losartan — Hepatic impairment

Based on pharmacokinetic data demonstrating significantly increased plasma concentrations of losartan in cirrhotic patients, a lower dose should be considered for patients with a history of hepatic impairment. Losartan must not be administered in patients with severe hepatic impairment. Losartan is not recommended in children with hepatic impairment.

Losartan — Renal impairment

Changes in renal function, including renal failure, have been reported as a consequence of inhibiting the renin-angiotensin system (particularly in patients with severe cardiac insufficiency or pre-existing renal dysfunction, or bilateral renal artery stenosis). Renal function should be regularly monitored during treatment. Concomitant use of losartan and ACE inhibitors has shown to impair renal function and is therefore not recommended.

Losartan — Dual RAAS blockade

Clinical trial data have shown that dual blockade of the RAAS through combined use of ACE inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent. LOSARGOOD AM H must not be used with aliskiren in patients with diabetes mellitus.

Losartan — Coronary and cerebrovascular disease

Excessive blood pressure decrease in patients with ischaemic cardiovascular and cerebrovascular disease could result in myocardial infarction or stroke.

Amlodipine — Hypotension

Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. Because of the gradual onset of action, acute hypotension is unlikely.

Amlodipine — Worsening angina / MI

Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of amlodipine, particularly in patients with severe obstructive coronary artery disease.

Amlodipine — Hepatic impairment

Because amlodipine is extensively metabolised by the liver with a plasma half-life of 56 hours in patients with impaired hepatic function, titrate slowly when administering to patients with severe hepatic impairment.

Hydrochlorothiazide — Hypotension and electrolyte/fluid imbalance

Symptomatic hypotension may occur. Periodic determination of serum electrolytes and creatinine should be performed. Thiazides can cause fluid or electrolyte imbalance including hypokalaemia, hyponatraemia and hypochloraemic alkalosis. Thiazides may decrease urinary calcium excretion and cause intermittent slight elevation of serum calcium. If hypercalcaemia occurs, further diagnostic tests are necessary. Thiazides should be discontinued before carrying out a test for parathyroid function. Thiazides increase urinary excretion of magnesium, which may result in hypomagnesaemia. Hyponatraemia accompanied by neurological symptoms has been seen in isolated cases.

Potassium monitoring: At 12.5 mg/day of hydrochlorothiazide, the decrease in serum potassium concentrations is on average 0.36 mmol/l after 6 months. Serum potassium concentration should be established at the start of treatment and after 3–4 weeks, then every 4–6 months if potassium balance is not affected by other factors. Concomitant treatment with oral potassium or a potassium-sparing diuretic can be

considered in patients receiving digitalis, with coronary heart disease symptoms, receiving high-dose beta-2 agonists, or with plasma concentrations <3.0 mmol/l. Combined treatment with hydrochlorothiazide and a potassium salt or potassium-sparing diuretic should be avoided in patients also receiving an ACE inhibitor.

Hydrochlorothiazide — Metabolic effects

Hydrochlorothiazide can increase serum uric acid; new episodes of gout are rarely seen. Hydrochlorothiazide must not be used as first-choice treatment for patients with manifest diabetes mellitus. Small, sometimes reversible increases in total cholesterol, triglycerides or LDL cholesterol have been reported. Hydrochlorothiazide is not to be used as first-choice treatment in patients receiving treatment for hypercholesterolaemia.

Hydrochlorothiazide — Non-melanoma skin cancer

An increased risk of non-melanoma skin cancer (basal cell carcinoma and squamous cell carcinoma) has been observed with increasing cumulative doses of hydrochlorothiazide. Patients taking hydrochlorothiazide should be advised to limit exposure to sunlight and UV radiation and to use adequate sun protection. Suspicious skin lesions should be examined promptly.

Lactose content

This medicinal product contains 30 mg lactose monohydrate per tablet. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sunset yellow (E110) content

This medicinal product contains sunset yellow (E110). Sunset yellow may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Losartan interactions

Potassium-raising agents (potassium-sparing diuretics, potassium supplements, potassium-containing salt substitutes, heparin):

May lead to increases in serum potassium. Co-medication is not advisable.

Fluconazole (CYP2C9 inhibitor):

Decreases exposure to the active losartan metabolite by approximately 50%. The clinical relevance is unknown.

Rifampicin (CYP inducer):

A 40% reduction in plasma concentration of the active metabolite was found. Clinical relevance unknown.

Other antihypertensives, tricyclic antidepressants, antipsychotics, baclofen, amifostine:

May increase the hypotensive action of losartan.

Lithium:

Reversible increases in serum lithium concentrations and toxicity have been reported with ARBs. If this combination proves essential, serum lithium level monitoring is recommended.

NSAIDs (including selective COX-2 inhibitors and aspirin at anti-inflammatory doses):

Attenuation of the antihypertensive effect may occur. Increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor pre-existing renal function. Adequate hydration and monitoring of renal function are recommended.

Amlodipine interactions

CYP3A inhibitors (moderate and strong):

Co-administration results in increased systemic exposure to amlodipine. Monitor for symptoms of hypotension and oedema.

CYP3A inducers:

Blood pressure should be closely monitored when amlodipine is co-administered with CYP3A inducers.

Sildenafil:

Monitor for hypotension when sildenafil is co-administered with amlodipine.

Simvastatin:

Co-administration of simvastatin with amlodipine increases systemic exposure to simvastatin. Limit simvastatin dose to 20 mg daily in patients on amlodipine.

Ciclosporin/Tacrolimus:

Amlodipine may increase the systemic exposure of ciclosporin or tacrolimus. Frequent monitoring of trough blood levels and dose adjustment are recommended.

Hydrochlorothiazide interactions

Agents associated with potassium loss and hypokalaemia (kaliuretic diuretics, glucocorticoids, ACTH, laxatives, carbenoxolone, amphotericin B, penicillin G sodium, salicylates and derivatives):

May enhance the potassium-depleting effect. Monitor potassium levels.

Lithium:

Concomitant application may lead to diminished lithium elimination and increased cardiotoxic and neurotoxic effects of lithium. Co-administration is not recommended.

ACE inhibitors:

Severe first-dose hypotension and deterioration of renal function may develop. Treatment with diuretics should be stopped 2–3 days before starting ACE inhibitor therapy.

NSAIDs and selective COX-2 inhibitors:

May diminish antihypertensive and diuretic effects of hydrochlorothiazide. Acute renal failure may occur in hypovolaemic patients. The risk of hospitalisation is doubled in patients treated with both NSAIDs and diuretics.

Other antihypertensives, barbiturates, alcohol, phenothiazines, tricyclic antidepressants, vasodilators, beta-blockers, nitrates:

May intensify the antihypertensive efficacy of hydrochlorothiazide.

4.6 Fertility, pregnancy and lactation

Pregnancy — Losartan

The use of losartan is not recommended during the first trimester of pregnancy. The use of losartan is contraindicated during the 2nd and 3rd trimesters of pregnancy. Exposure to AIIRA therapy during the 2nd and 3rd trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia). Should exposure to losartan have occurred from the second trimester, ultrasound check of renal function and skull is recommended. When pregnancy is diagnosed, treatment with losartan should be stopped immediately.

Breast-feeding — Losartan

Because no information is available regarding the use of losartan during breast-feeding, losartan is not recommended. Alternative treatments with better-established safety profiles are preferable, especially while nursing a newborn or preterm infant.

Pregnancy — Amlodipine

Animal data with amlodipine in rats and rabbits provide no evidence of a teratogenic effect. However, there is no clinical experience with the preparation in pregnancy. Accordingly, amlodipine should not be administered during pregnancy or to women of childbearing potential unless effective contraception is used.

Breast-feeding — Amlodipine

There is no clinical experience with amlodipine in lactation. Amlodipine should not be administered during breast-feeding.

Pregnancy — Hydrochlorothiazide

Experience with hydrochlorothiazide during pregnancy is limited, particularly during the first trimester. Hydrochlorothiazide crosses the placenta. Its use during the 2nd and 3rd trimesters may compromise foeto-placental perfusion and may cause foetal and neonatal effects (icterus, electrolyte disturbance, thrombocytopenia). Hydrochlorothiazide should not be used for gestational oedema, gestational hypertension or pre-eclampsia. It should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.

Breast-feeding — Hydrochlorothiazide

Hydrochlorothiazide is excreted in human milk in small amounts. If hydrochlorothiazide is used during breast-feeding, doses should be kept as low as possible.

Fertility

Animal studies with hydrochlorothiazide indicated no harmful effects on fertility or reproduction. No human data regarding effect on fertility are available for this combination.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. When driving vehicles or operating machines, it must be borne in mind that dizziness or drowsiness may occasionally occur with antihypertensive therapy, particularly during initiation of treatment or when the dose is increased.

4.8 Undesirable effects

Summary of the safety profile

The adverse reaction profile of LOSARGOOD AM H reflects the individual profiles of losartan, amlodipine and hydrochlorothiazide. The most common adverse reactions include headache, dizziness, fatigue, asthenia and peripheral oedema. The most serious adverse reactions include angioedema, acute renal failure, hypotension, hepatotoxicity and non-melanoma skin cancer.

Tabulated list of adverse reactions
Frequencies from the individual components. Within each SOC, adverse reactions are listed in order of decreasing seriousness.

System Organ Class / Component	Common	Uncommon	Rare / Very Rare / Not Known
Blood & lymphatic — HCT	Thrombocytopenia (HCT)	Leukopenia (HCT)	Agranulocytosis, aplastic anaemia, haemolytic anaemia (HCT — very rare); anaemia, Henoch-Schönlein purpura, ecchymosis, haemolysis (losartan)
Immune system — Losartan/HCT			Anaphylactic reactions, angioedema, urticaria (losartan — rare); hypersensitivity reactions (HCT — rare)
Metabolism — HCT	Electrolyte disturbances (hypokalaemia, hyponatraemia, hypochloraemia, hypercalcaemia), hyperglycaemia, glucosuria, hyperuricaemia, elevated serum lipids (HCT — very common/common)	Anorexia, gout (losartan)	
Psychiatric disorders	Insomnia (losartan, amlodipine)	Anxiety, depression, abnormal dreams, somnolence, memory impairment (losartan); anxiety, depression, insomnia, nervousness (amlodipine)	
Nervous system disorders	Headache, dizziness (losartan)	Nervousness, paraesthesia, peripheral neuropathy, tremor, migraine, syncope (losartan); hypoaesthesia, neuropathy peripheral, paraesthesia, tremor, vertigo (amlodipine); paraesthesia, headache, dizziness (HCT — rare)	Cerebrovascular event (losartan — uncommon)
Eye disorders		Blurred vision, burning/stinging, conjunctivitis, decreased visual acuity (losartan)	Visual disorders, blurred vision, xanthopsia, aggravation of myopia (HCT); acute myopia, acute angle-closure glaucoma (HCT — not known)

System Organ Class / Component	Common	Uncommon	Rare / Very Rare / Not Known
Ear and labyrinth		Vertigo, tinnitus (losartan); tinnitus (amlodipine)	
Cardiac disorders	Palpitations (HCT)	Hypotension, orthostatic hypotension, angina pectoris, AV block, myocardial infarction, palpitations, arrhythmias (losartan); arrhythmia, bradycardia, tachycardia, chest pain (amlodipine)	Arrhythmias (HCT — rare)
Vascular disorders		Vasculitis (losartan/amlodipine)	Necrotizing vasculitis (HCT — very rare)
Respiratory disorders		Dyspnoea, epistaxis (amlodipine)	Respiratory distress, interstitial pneumonia (HCT — uncommon); pulmonary oedema with shock (HCT — very rare)
Gastrointestinal disorders	GI disorders including nausea, vomiting, diarrhoea, abdominal pain (HCT)	Anorexia, constipation, diarrhoea, flatulence, pancreatitis, vomiting, gingival hyperplasia (amlodipine)	Constipation (HCT — rare)
Hepatobiliary disorders		Pancreatitis, cholestatic jaundice (HCT)	Liver injury (amlodipine — rare)
Skin and subcutaneous tissue disorders		Allergic skin reactions: pruritus, erythema, photoallergic exanthema, purpura, urticaria (HCT); angioedema, erythema multiforme, pruritus, rash (amlodipine)	TEN, cutaneous lupus erythematosus, lupus erythematosus-like reactions (HCT — very rare); non-melanoma skin cancer (HCT — not known)
Renal and urinary disorders	Glucosuria, reversible elevation of serum creatinine and urea (HCT)	Interstitial nephritis (HCT)	Renal failure (renal function changes as consequence of RAAS inhibition — losartan — very rare)
Reproductive disorders		Impotence (HCT); decreased libido, impotence (losartan)	Sexual dysfunction (amlodipine)
General disorders	Asthenia, fatigue, chest pain (losartan); peripheral oedema (amlodipine)	Facial oedema (losartan); back pain, malaise (amlodipine)	Drug fever (HCT)
Neoplasms			Non-melanoma skin cancer (basal cell carcinoma, squamous cell carcinoma — HCT — not known)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose

Losartan

The most likely manifestation of overdose would be hypotension and tachycardia; bradycardia could occur from parasympathetic stimulation. If symptomatic hypotension occurs, provide supportive treatment. Administer activated charcoal after oral intake and monitor vital parameters closely. Neither losartan nor the active metabolite can be removed by haemodialysis.

Amlodipine

Gross overdosage could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and prolonged systemic hypotension, up to and including shock with fatal outcome, has been reported. Clinically significant hypotension calls for active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities, attention to circulating fluid volume and urine output. A vasoconstrictor may be helpful. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.

Hydrochlorothiazide

Symptoms: acute fluid loss, gastrointestinal symptoms, polyuria or oliguria, dizziness, impaired consciousness, hypokalaemia (muscle weakness, fatigue, cardiac arrhythmias, hypotension, coma) and acute hyponatraemia (agitation, headache, convulsions). Treatment: induce vomiting, repeated administration of activated charcoal and large amounts of fluid. Maintain fluid and electrolyte balance. Potassium supplementation where necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II antagonists and calcium channel blockers and diuretics. ATC codes: Losartan: C09CA01; Amlodipine: C08CA01; Hydrochlorothiazide: C03AA03.

Losartan

Losartan is a synthetic oral angiotensin-II receptor (type AT1) antagonist. By selectively blocking the AT1 receptor, losartan blocks all physiologically relevant actions of angiotensin II (vasoconstriction, aldosterone release, smooth muscle cell proliferation) without agonist effects and without inhibiting ACE. Removal of the angiotensin II negative feedback leads to increased plasma renin activity, but antihypertensive activity and suppression of plasma aldosterone concentration are maintained. The active metabolite E-3174 is 10- to 40-times more active than losartan on a weight-for-weight basis.

Amlodipine

Amlodipine is a dihydropyridine calcium channel antagonist that inhibits transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Amlodipine selectively inhibits calcium ion influx with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. It is a peripheral arterial vasodilator that reduces peripheral vascular resistance and blood pressure. Negative inotropic effects have been detected in vitro but have not been seen in intact animals at therapeutic doses. Serum calcium concentration is not affected by amlodipine. Amlodipine has a gradual rate of association and dissociation with the calcium channel receptor, resulting in a gradual onset of effect.

Hydrochlorothiazide

Thiazide diuretics exert their effect in the distal part of the renal tubule by inhibiting NaCl resorption. The increased amount of Na+ and water in the collecting duct results in increased secretion and excretion of K+ and H+. Diuresis is promoted after administration of 12.5 mg in subjects with normal renal function. The diuretic and natriuretic effect is noticeable 1–2 hours after oral administration, reaches its maximum after 4–6 hours and can last for 10–12 hours. With long-term administration, the antihypertensive effect of hydrochlorothiazide is dose-related between 12.5 and 50 mg/day. Combined treatment with other antihypertensive agents increases the blood pressure-lowering effect.

5.2 Pharmacokinetic properties

Losartan

Absorption: Well absorbed after oral administration; systemic bioavailability approximately 33%. Cmax of losartan and active metabolite reached in 1 hour and 3–4 hours, respectively. Distribution: Both losartan and its active metabolite are ≥99% protein bound. Volume of distribution of losartan is 34 litres. Metabolism: Approximately 14% of oral dose converted to the active carboxylic acid metabolite. Elimination: Plasma clearance approximately 600 ml/min (losartan) and 50 ml/min (active metabolite). Terminal half-life: approximately 2 hours (losartan) and 6–9 hours (active metabolite). Approximately 4% excreted unchanged in urine; 6% as active metabolite. Neither losartan nor the active metabolite is removed by haemodialysis.

Amlodipine

Absorption: Peak plasma concentrations reached 6–12 hours after oral dosing. Absolute bioavailability 64–90%. Bioavailability not altered by food. Distribution: Approximately 93% protein bound. Biotransformation: Extensively (approximately 90%) converted to inactive metabolites via hepatic metabolism; 10% of the parent compound and 60% of the metabolites excreted in urine. Terminal elimination half-life approximately 30–50 hours. Steady state reached after 7–8 days. The pharmacokinetics of amlodipine are not significantly influenced by renal impairment. Elderly patients and patients with hepatic insufficiency have decreased clearance of amlodipine (AUC increased by approximately 40–60%).

Hydrochlorothiazide

Absorption: Total absorption around 70% of the dose. Bioavailability is directly proportional to dose. Distribution: Accumulates in erythrocytes; maximum concentration approximately 4 hours after oral administration. Plasma protein binding 40–70%; apparent volume of distribution 5–6 l/kg. Crosses the placenta; excreted in maternal milk. Elimination: Plasma half-life 9.5–13 hours. Within 72 hours, 60–80% of an oral dose is excreted in urine, 95% unchanged. In elderly patients, steady-state concentration is elevated and systemic clearance significantly decreased.

5.3 Preclinical safety data

Losartan

Preclinical data reveal no special hazard for humans based on conventional studies of general pharmacology, genotoxicity and carcinogenic potential. Like other substances that directly affect the renin-angiotensin system, losartan has been shown to induce adverse reactions on late foetal development, resulting in foetal death and malformations.

Amlodipine

Rats and mice treated with amlodipine maleate for up to two years showed no evidence of a carcinogenic effect. Mutagenicity studies revealed no drug-related effects at either the gene or chromosome level. No effect on fertility was observed in rats at doses up to 10 mg amlodipine/kg/day.

Hydrochlorothiazide

Sub-chronic and chronic toxicity studies in dogs and rats revealed changes in electrolyte balance only. In vitro and in vivo mutagenicity assays showed negative results. Long-term carcinogenicity studies showed no relevant elevations of tumour amount. Animal studies showed no effects on fertility in rats and no teratogenic effects in rats, mice and rabbits.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The following excipients are present in the film-coated tablet:

No.	Ingredient
1	Lactose monohydrate (excipient with known effect — 30 mg per tablet)
2	Microcrystalline cellulose
3	Maize starch
4	Hydroxypropylmethylcellulose (HPMC)
5	Purified water
6	Purified talc
7	Colloidal anhydrous silica
8	Crospovidone
9	Magnesium stearate
10	Isopropyl alcohol
11	Titanium dioxide (E171)
12	Sunset yellow (E110) (excipient with known effect)
13	Mono propylene glycol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store at a temperature not exceeding 30°C. Protect from light and moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container
1 ALU-ALU blister of 10 tablets; 3 such blisters packed in printed carton with package insert. Pack size: 30 tablets.

6.6 Special precautions for disposal and other handling
No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
ZAIN PHARMA LTD.

Plot No. 209/13741, Colchester Park,

Go-Down No. 1, 2, 3, Off Mombasa Road,

Behind Nice and Lovely House,

P.O. Box: 100167-00101, Nairobi, Kenya.

8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)
H2025/CTD12489/26435

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